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Reconstructive Strategies in Pediatric Patients after Oncological Chest Wall Resection: A Systematic Review

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Keywords

- \blacktriangleright chest wall reconstructions
- ► chest wall tumors
- ► reconstructive surgery
- ► pediatric surgery

Abstract An appropriate reconstruction strategy after surgical resection of chest wall tumors in children is important to optimize outcomes, but there is no consensus on the ideal approach. The aim of this study was to provide an up-to-date systematic review of the literature for different reconstruction strategies for chest wall defects in patients less than 18 years old. A systematic literature search of the complete available literature was performed and results were analyzed. A total of 22 articles were included in the analysis, which described a total of 130 chest wall reconstructions. All were retrospective analyses, including eight case reports. Reconstructive options were divided into primary closure ($n = 21$ [16.2%]), use of nonautologous materials ($n = 83$ [63.8%]), autologous tissue repair ($n = 2$ [1.5%]), or a combination of the latter two ($n = 24$ [18.5%]). Quality of evidence was poor, and the results mostly heterogeneous. Reconstruction of chest wall defects can be divided into four major categories, with each category including its own advantages and disadvantages. There is a need for higher quality evidence and guidelines, to be able to report uniformly on treatment outcomes and assess the appropriate reconstruction strategy.

Introduction

Pediatric tumors are rare, with chest wall tumors (CWT) being even more rare, accounting for 1.8% of all solid tumors in children.¹ CWT can be benign, but the majority is malignant, with Ewing sarcomas occurring the most, followed by osteosarcomas, rhabdomyosarcomas, and other sarcomas.²⁻⁴ Treatment often requires a multidisciplinary approach involving (neo)adjuvant chemotherapy and surgical resection of all affected ribs, as well as adjacent ribs to

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accomplish radical resection. Larger chest wall defects (CWD) require a reconstruction to maintain physiological function and aesthetic appearance. Several studies have described outcomes of different reconstruction strategies.^{5–7} While these studies give a good impression of what to expect of a specific resection of a specific area of the chest at a certain age, these reports are often based on small singlecenter studies. Interpretation of the results is hampered by the lack of standardized reconstruction methods, the use of

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diverse outcome measures, and by combining the results of different anatomic regions and age categories. This causes lack of consensus on the ideal approach, with regard to reconstructive materials and techniques. Furthermore, pediatric patients pose an additional challenge regarding their growing and developing body and the need to prevent growth deformities and impaired function.

To date, no systematic literature review on this matter has been published. Sandler and Hayes-Jordan have published an informative expert opinion article including an interpretation of selected studies. 8 However, it does not include a quantifiable overview of outcomes on this specific subject. Moreover, as new reconstructive techniques develop fast, there is a need to reassess the literature on this subject.^{9,10}

In this study, it is our aim to systematically present the current knowledge on this matter, providing clinicians up to date recommendations, and creating a fundament for the development of guidelines and future improvements in the different reconstructive options in children with CWD.

Methods

Search Strategy

This systematic review of literature was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹¹ The PubMed and Embase databases were searched on studies that reported on patients with CWD treated with any type of reconstruction, published between 2002 and February 2022. Key search terms included "chest wall defects" and "children" in combination with the keywords "surgery," "surgical treatment," and "reconstructive surgical procedures," "allografts," "bio grafts," and "surgical flaps." After removal of duplicates, title and abstract screening was performed independently by two investigators (P.W.L. and Z.N.O.) based on predetermined criteria (see below). Any disagreement was resolved using arbitration by a third author (E.C.P.), after which the full-text articles were analyzed. Backward and forward snowballing of references of included studies was performed.

Study Selection

Studies were included if all three of the inclusion criteria were met: (1) the study included at least one pediatric patient $(< 18$ years old) with a CWD, treated by any type of reconstruction. When a study described both pediatric and adult patients, only the pediatric data were included; (2) the method of reconstruction was described for each patient; and (3) the outcome was reported for each reconstruction method.

Data Extraction

Predetermined data were extracted and study strength was determined using the MINOR (Methodological Index for Non-Randomized Studies) criteria.¹² If available, the following items were extracted: first author, year of study, region, location of defect, reconstruction method

(primary closure, autologous or non-autologous) number of patients, age, number of ribs resected, follow-up duration and complications.

Statistical Analysis

Categorical data are presented as proportions and continuous data are reported as mean \pm standard deviation or median (interquartile range [IQR]), depending on the normality of the distribution. Analyses were conducted with SPSS (IBM SPSS Statistics, version 25).

Results

Search Outcomes

The initial database search of PubMed Medline yielded 130 records. After removing duplicates and elimination by title and abstract and full text review, 22 studies were included. The selection process, based on the PRISMA guidelines, is detailed in ►Fig. 1. Eight articles were case-reports.¹³⁻²⁰ The other 14 articles were retrospective evaluations of outcomes and complications after the use of new reconstructive materials or techniques.

Overview of Studies

An overview of all included studies and their characteristics can be found in ►Table 1. The quality of studies assessed by the MINOR tool was rather low, with a median score of 8 (IQR: 6–9), ranging from 0 to 16. The total number of patients who underwent a chest wall resection and reconstruction was 130, with an overall median age of 10.7 years (IQR: 6.4–12.9). An overall median of 3.0 ribs (IQR: 2.0–3.6) was resected. Overall median follow-up was 30.8 months (IQR: 23.1–39.1). CWD on the posterior chest wall occurred the most $(n = 38$ [29.2%]), followed by the anterior chest wall ($n = 22$ [16.9%]). In 40.8% of the patients ($n = 53$), CWD location was unknown (\sim Table 2). Data concerning CWD size were missing for the vast majority of the included studies.

Reconstruction Strategies

The type of reconstruction was subdivided into four categories: primary closure $(n=21 \; [16.2\%])$, nonautologous $(n = 83 \; [63.8\%])$, autologous $(n = 2 \; [1.5\%])$, or combined $(n = 24 \mid 18.5\%)$ (\sim Table 2). The latter consisted of patients where both autologous (i.e., muscle flaps) and nonautologous materials were used. When there was no indication for grafts due to a small defect size, only primary wound closure was performed. Small defect size is defined as a CWD consisting of less than two ribs or smaller than 5 cm.²¹ Nonautologous materials were subdivided into three categories: synthetic materials $(n = 80 \; [66.1\%])$, bioprosthetic materials ($n = 19$ [15.7%]), and rigid materials $(n = 22$ [18.2%]).

The different kind of grafts mentioned in the analyzed literature are shown in \rightarrow Table 3. Most of the synthetic materials are flexible meshes, including nonabsorbable meshes such as polytetrafluoroethylene (Gore-Tex) and polypropylene (Prolene or Marlex), and absorbable meshes

Fig. 1 Flow diagram of study selection.

such as polyglactin (Vicryl) and L-lactic acid with glycolic acid copolymer plates (LactoSorb). Bioprosthetic grafts mostly consisted of porcine small intestinal submucosa (SIS/Biodesign), porcine dermis (Permacol), and bovine pericardium (Tutopatch). Rigid materials include the Vertical Expandable Prosthetic Titanium Rib (VEPTR), STRATOS titanium bars, MatrixRIB, and regular titanium plates. When a flexible Marlex mesh was strengthened with methyl methacrylate plates to provide more rigidity, it was categorized as rigid. The most frequently used combination of nonautologous and autologous methods was a Gore-Tex patch and latissimus dorsi flap, $(n = 36 [21.4\%])$ and $(n = 14 [8.3\%])$ respectively. In some cases, multiple nonautologous grafts were used in one single reconstruction (e.g., Gore-Tex patch combined with the titanium STRATOS bar), whether or not accompanied by an autologous tissue reconstruction. Except for the two not specified muscle flaps from Lopez et al, all autologous tissue graft reconstructions were combined with nonautologous material.⁷ Definitive conclusions regarding superiority of certain reconstructive methods over others were not able to be drawn. In the analyzed studies, the type of reconstruction did not influence the overall survival of the patients. A summary of the literature analysis is depicted in \blacktriangleright Fig. 2.

Complications

Deformities

Scoliosis was the most frequently mentioned complication $(n = 12 [9.2\%])$. Among the patients who developed scoliosis, four were treated with LactoSorb, others were treated with synthetic meshes ($n = 5$), SIS ($n = 1$), methyl acrylate sandwich $(n = 1)$, or not specified $(n = 1)$. Six of the twelve scoliosis cases needed additional surgery. All of these six patients had a tumor in the posterior section of the chest wall.

Infectious and Other Complications

Wound infection ($n = 3$ [2.3%]) and seroma formation ($n = 1$) [0.8%]) were present in two articles, as all other articles reported zero (graft-related) infectious complications. The wound infections occurred after placement of Gore-Tex patches and both were treated conservatively with antibiotics. Seroma formation occurred in a patient who underwent a combined Gore-Tex patch and STRATOS bar reconstruction, which was treated by aspiration. Dislocation of a titanium STRATOS bar was mentioned in one patient (0.8%), after which graft removal was necessary after

Table 1 Study characteristics

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prosthetic titanium rib.

Abbreviation: IQR, interquartile range.

7 months follow-up. One study described more postoperative pain and discomfort in patients whose CWD was reconstructed with methyl methacrylate plates.⁷ Some studies briefly reported on aesthetics and functionality, such as "good cosmetic results" or "little chest wall deformity." However, no patient-reported outcomes obtained by validated questionnaires were mentioned.

Discussion

In this systematic review, we provide an overview of the variety of methods and materials for the reconstruction of CWD in the pediatric population after oncological chest wall resection. Nonautologous materials were used most frequently (63.8%) with synthetic materials being the largest subcategory (66.1%). However, due to the heterogeneity of data, small study populations, and lack of long-term followup, it is not possible to draw firm conclusions regarding superiority of a certain reconstructive method over another. Even though the literature in the adult population is of higher quality, it also lacks standardized treatment protocols, as Colella et al reported in a recent systematic review.²² Hence, currently most appropriate reconstructive strategies are determined for each individual case, considering multiple patient- or surgeon-related factors.²³ Still, a consensus on the ideal approach based on location and size of the CWD and age

of the patient is lacking. Currently used reconstructive strategies are similar for both the adult and pediatric populations.8,24,25 However, due to the distinct differences between the adult- and pediatric population, with children having the additional challenge of a growing skeleton, reconstructive strategies for adults cannot simply be applied to children.

The ultimate reconstruction technique in children provides both sufficient rigidity to prevent paradoxical chest movements and to protect vital organs, as well as malleability to adjust to and mimic the contour of the thoracic wall. Lastly, it should be adaptive to the growing skeleton.²⁶ Important factors to determine the most suitable reconstruction strategy are size and location of the defect. For example, anterolateral defects should not be reconstructed with meshes alone because of their likelihood to cause paradoxical breathing and inadequate protection of vital organs.24,27 Apical-posterior defects reaching lower than the fourth rib posteriorly, irrespectively of size, should not be closed primarily but reconstructed with a graft, additionally considering possible scapular tip entrapment during movement of the arm. $21,25$ The authors believe that resection of the scapular tip could be considered in the case of expected scapular entrapment. Some grafts such as methyl methacrylate or osseous bone grafts are not radiolucent, which might be less suitable when adjuvant radiotherapy is indicated. Radiotherapy does not seem to affect the choice of reconstruction method so far described in the current literature. Also, there is no evidence about different reconstruction options after additional pulmonary resection.

Nonautologous Materials

In our analysis, 83 patients (63.8%) were treated with nonautologous materials alone, with synthetic grafts being the largest subcategory. Synthetic grafts are widely used and known for their relative ease of use, their ability to be fashioned to patient-specific dimensions intra-operatively, and their radiolucency.²⁸ A common disadvantage of meshes is the possibility to flail when the mesh is not pulled taut. Also mentioned in the literature is the need for additional autologous or nonautologous grafts in anterior or large defects because of their lacking strength.^{24,26} The nonabsorbable meshes also have the potential disadvantage of the necessity for removal in case of infection; however, this did not occur in any of the analyzed studies. Absorbable meshes such as Dexon or Vicryl are permeable to fluids and able to release periprosthetic fluid collections.²⁹ In the adverse case of an infection, it is possible to treat the patient conservatively with antibiotics without the need for removal of the mesh. Absorbable meshes are entirely absorbed in 3 to 6 months.³⁰ L-lactic acid and glycolic acid (LactoSorb) are a fully resorbable material and broadly used in children for craniofacial reconstructions, keeping its strength for a period up to 6 weeks, which is considered adequate for healing. After 9 to 15 months, the graft is entirely integrated that provides a more durable and stable reconstruction during growth than the before-mentioned materials.³¹

Table 3 Reconstruction materials

Note: All materials used for chest wall defect reconstruction organized per category (nonautologous, autologous or no graft). The nonautologous category is subdivided into three groups (synthetic, bioprosthetic or rigid).

Bioprosthetic grafts are either made of homografts (i.e., human cadaver) or xenografts (i.e., bovine or porcine). Consisting of decellularized collagen matrices, they are able to suppress an inflammatory response, subsequently allow vascular and cellular infiltration, and eventually graft integration.29,32,33 Early cellular infiltration, in the first place by macrophages and mast cells, is essential for graft integration. Proliferation of blood vessels is initiated simultaneously. The secretion of cytokines attracts fibroblasts, which allows collagen deposition and eventually graft integration.³² Oliveira et al found out that bioprosthetic grafts appear to be a suitable solution for CWD in growing children.³⁴ However, long-term effectiveness and strength need to be further assessed. A study investigating bioprosthetic meshes in rats found 100% neocellularity 3 months after surgery.³⁵ Other bioprosthetic characteristics are similar to synthetic grafts, sharing the aforementioned advantages and disadvantages. Furthermore, bioprosthetic grafts are relatively

Fig. 2 Summary of the literature analysis.

expensive; thus, long term outcomes need to be further investigated in future studies to assess cost-effectiveness.³⁶

Rigid materials are suitable for larger defects according to some studies, restoring the rigidity of the thoracic wall, and offering an ideal scaffold for meshes and musculocutaneous autologous flap reconstruction.^{37–39} Risk of complications such as dislocation, thoracic pain, and plate fracture needs to be taken into account when this strategy is considered. Furthermore, the rigid character conflicts with the aforementioned ideal quality of being adaptive to growth. However, VEPTR is an expandable device, which bridges the CWD by anchoring to the superior and inferior ribs and can be expanded when indicated. The use of VEPTR for CWD is considered off-label but appears to deliver structural support in growing children without the incidence of complications, as seen in our analysis. $6,41$

Scoliosis

Scoliosis is one of the most common long-term complications, possibly caused by the absence of stability and counter pressure of the ribs and therefore with the convexity on the ipsilateral side.⁴² Yet, the exact etiology remains still unknown. The reported incidence is quite heterogeneous, reported to be between 13 and 52% after a mean follow-up between 6.4 and 10 years.⁴²⁻⁴⁵ In the analyzed literature, we found the presence of scoliosis in 9.2% of the patients, probably as a consequence of the relatively short overall median follow-up. The scoliosis incidence was not affected by the method of reconstruction, according both the literature and our analysis. However, Scalabre et al were able to describe prognostic factors for the development of scoliosis, such as the number of resected posterior ribs being more than two and undergoing surgery during a rapid growth period.⁴⁴ Rapid growth period is defined as the age of less than 6 years and between 12 and 15 years old. In addition, CWD superior to the sixth rib is associated with an increased incidence of scoliosis.⁴⁵ In the analyzed studies of the current

review, all of the six patient who developed scoliosis had a tumor in the posterior section of the chest wall. According to the literature, radiotherapy was not associated with a higher incidence of scoliosis.⁴⁴ Spinal arthrodesis can be considered to prevent scoliosis, based on the number of resected ribs and/or vertebrae involvement. 8 Jackson et al described two cases with CWD with two and five resected ribs, respectively, and used the STRATOS titanium bar for the first time in the pediatric population, with promising results.⁴⁶ Long-term follow-up has to determine whether scoliosis can be prevented in children by certain measures, such as Jackson et al suggested. The two patients in this study had none of the risk factors for scoliosis development, which were mentioned earlier in this paragraph. It remains questionable if these patients would have developed scoliosis when less rigid materials were used.

Limitations

There are several limitations to this study that needs be taken into account. Due to the rarity and complexity of the subject, there is a scarcity of high-quality studies. All studies were retrospective analyses with a substantial number of case reports, in which patient characteristics were poorly described. Also, the aforementioned important factor "CWD size" of the CWD was not available in most of the studies. Nevertheless, we were able to retrieve the median number of resected ribs of the vast majority of the articles, which provides a satisfactory indication of the defect size. As a consequence of these missing and heterogeneous data, meta-analyses were not possible.

Future Perspectives

Future perspectives regarding reconstructive materials are promising. First, there is three-dimensional (3D) printing of customized bio-scaffolds, consisting of a combination materials where both rigidity and biodegradability can be achieved.⁴⁷ Pontiki et al treated adult patients with 3D-

printed patient-specific rigid grafts, and report an improved quality of life and cosmetic results, compared with nonrigid grafts.⁴⁸ Second, tissue engineering has successfully been used to reconstruct CWD in animal studies using adipose stem cells.⁴⁹ Tang et al were able to effectuate new bone generation in canine models using biodegradable meshes and demineralized bone matrix with bone marrow mesenchymal stem cells, resulting in regenerated bone defects after 24 weeks.⁵⁰ While assessment of the long-term outcome is necessary before clinical use can be considered, use of such materials might address the issue of growth and development in the pediatric population.

Conclusion

CWD reconstruction techniques can be divided into four major categories, with each category having its own advantages and disadvantages. Lack of high-quality studies and due to data heterogeneity, superiority of one technique over another cannot be determined. There is a need for highquality studies to assess treatment algorithms. The development of new reconstruction materials using 3D printing and tissue engineering is promising.

Conflict of Interest

None declared.

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